REMARKS

I. Status of Claims

Claims 1-20 are pending in this application.

In the present amendment, claims 1-10, 12-17, and 20 have been amended to more appropriately claim the invention, and to correct informalities. In addition, new claims 21-48 have been added to more appropriately claim the invention. Support for new claims 21-48 can be found in the original claims 1-20 and the specification of the present invention.

Applicants have not introduced any new matter by the amendment, nor are any estoppels intended thereby. Further, the amendment does not raise new issues or necessitate the undertaking of any additional search of the art by the Office.

II. Rejection under 35 U.S.C. § 112, Second Paragraph

The Office rejected claims 12-16 and 20 under 35 U.S.C. 112, second paragraph, "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention," for the following four reasons:

(1) Claims 12-16 are improperly dependent on claims 6-10;

(2) The term "diabetes complications" is not clearly defined and both the broader citation of "diabetes complications" and the narrower citation of "nephropathy and retinopathy" are included in a same claim;

(3) The diseases of "restricted memory performance or a restricted ability to learn" are not clearly defined; and

(4) The term "appropriate acid or acid chloride" in claim 20 is not clearly defined. Office Action, pages 2 and 3.

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

To overcome this rejection, Applicants respectfully submit the following amendments and remarks:

(1) Applicants amended claims 12-16 as shown above. Specifically, Applicants amended claim 12 to be in an independent form reciting compounds of claim 6, and amended claims 13-16 to be dependent on claim 12 and to recite compounds of claims 7-10, respectively.

(2) Applicants amended claim 12 as shown above. Specifically, Applicants deleted the phrase "nephropathy and retinopathy" from claim 12, and moved it to a new dependent claim 22 thereof.

(3) Applicants amended claim 12 as shown above. Specifically, Applicants amended the phrase "restricted memory performance or a restricted ability to learn" to "diseases with symptoms of restricted memory performance and/or a restricted ability to learn".

(4) Applicants amended claim 20 as shown above. Specifically, Applicants amended the term "an appropriate acid or acid chloride" to "a respective acid or acid chloride." As disclosed, for example, in paragraphs [0115], [0116], [0223], and [0236] of the specification, the process of claim 20 comprises forming an amide bond by reaction of the respective 1,2,3,4-tetrahydronaphthylamine with the respective acid of the formula R^5-COOH or acid chloride of formula R^5-COCl under reaction conditions. Therefore, the term "a respective acid or acid chloride" is definite and can be readily understood by one of ordinary skill in the art.

Accordingly, Applicants respectfully request this rejection be withdrawn.

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

III. Rejections under 35 U.S.C. § 102(b)

A. Beasley et al.

The Office rejected claims 1-4, 6-9, 11-15, and 17-20 under 35 U.S.C. § 102(b) as being anticipated by Beasley et al. (WO 97/04775) ("*Beasley*"). Office Action, pages 3 and 4. Specifically, the Office contended that "[t]he instantly claimed compounds read on reference disclosed compounds, see formula (I) in page 4 and the species of Examples 5 and 6." *Id.* at page 3. The Office further contended that *Beasley* "discloses that the compounds have therapeutic effect on various diseases of mammal, including asthma, diabetes insipidus, stroke, etc. (see page 7, starting at line [] 23)" and because "[t]he therapeutic effect of claims 6-9 is evident from the dependent claim[s] 12-15," "the instantly claimed mechanism of stimulating the expression of endothelial NO-synthase is inherently taught in the reference." *Id.* at page 4. Applicants respectfully disagree for at least the following reason.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." M.P.E.P. § 2131 (quoting *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987)) (emphasis added).

The compounds of formula (I) disclosed in *Beasley* at page 4, as well as specific examples 5 and 6 mentioned by the Office, do not contain the group corresponding to R^5 of the compounds claimed in the present invention, for example, in claims 1 and 6. In formula (I) of the present invention, R^5 is bonded to the C=O group of the NH-CO moiety. R^5 is a group Ar or a group Hetar, wherein the group Ar is phenyl, naphth-1-yl or naphtha-2-yl, and the group Hetar is an aromatic ring. *See e.g.*, claims 1 and 6.

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

Therefore, the R^5 group of compounds of formula (I) in the present invention is an aromatic ring, which comprise a conjugated cyclic system of six pi electrons.

However, in the compounds of formula (I) of *Beasley*, the ring, which is bonded to the C=O group of the NH-CO moiety, cannot be an aromatic ring, because of the mandatory presence of the C=Y group (wherein Y is O or S) in the ring and the substituent group R^1, which does not include hydrogen, on the nitrogen atom of the ring. *See Beasley*, page 4. Such a ring structure makes it impossible for a conjugated cyclic system of six pi electrons to exist. A conjugated cyclic system of six pi electrons could only exist theoretically by creating, in an energetically unfavorable manner, opposite electrical charges within the molecule to give arise to a positively charged part and a negatively charged part. Therefore, as the compounds of *Beasley* do not contain the group corresponding to group R^5 of the compounds of the present invention, *Beasley* does not anticipate the presently claimed invention.

Accordingly, Applicants respectfully request this rejection be withdrawn.

B. Niewöhner et al.

The Office rejected claims 1, 18, and 19 under 35 U.S.C. § 102(b) as being anticipated by Niewöhner et al. (EP 0253257) ("*Niewöhner*"). Office Action, page 4. Specifically, the Office contended that that "[t]he instantly claimed compounds read on reference disclosed compounds, see compounds 18 and 21 in Table 1 (page 14)." *Id.*

Applicants have amended claim 1 to include an additional proviso that "where one of the groups R^1 and R^2 is hydroxy and the other groups of R^1, R^2, R^3, and R^4 are hydrogen, R^5 is not unsubstituted pyridyl." Claims 18 and 19 are dependent on claim 1. Therefore, Applicants respectfully request this rejection be withdrawn.

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

C. Horn et al.

The Office rejected claims 6-9, 11-15, and 17 under 35 U.S.C. § 102(b) as being anticipated by Horn et al. (EP 0420064) ("*Horn*"). *Id.* at page 4. Specifically, the Office contended that "[t]he reference discloses 2-amidotetralin derivatives (see formula in page 3 wherein R4 is aryl and the compounds of Examples 3 and 14) and the reference discloses that the compounds have therapeutic effect on various diseases of mammal, including sexual dysfunction, etc. (see page 5, lines 6-22)" and because "[t]he therapeutic effect of claims 6-9 is evident from the dependent claims 12-15," . . . "the instantly claimed mechanism of stimulating the expression of endothelial NO-synthase is inherently taught in the reference." *Id.*

In addition, the Office rejected claims 6-17 under 35 U.S.C. § 102(b) as being anticipated by *Horn*. *Id.* at pages 4 and 5. Specifically, the Office contended that "[t]he reference discloses amide compounds (see formula (I) in page [3] and the species of Example 6) and the reference discloses that the compounds have therapeutic effect on various diseases, including stroke, etc. (see page 1, lines 18+)" and because "[t]he therapeutic effect of claims 6-9 is evident from the dependent claims 12-15," "the instantly claimed mechanism of stimulating the expression of endothelial NO-synthase is inherently taught in the reference." *Id.*

Applicants respectfully disagree with these rejections for at least following reasons.

First, Applicants respectfully submit that we cannot find the teaching in *Horn* that its compounds "have therapeutic effect on various diseases, including stroke, etc. (see page 1, lines 18+[,]" as contended by the Office.

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

Second, the Office has failed to provide any evidence to support its contention that "the instantly claimed mechanism of stimulating the expression of endothelial NO-synthase is inherently taught in the reference." *Horn* nowhere discloses that its compounds can stimulate the expression of endothelial NO-synthase. Instead, *Horn* clearly teaches that the compounds disclosed therein can treat diseases by their "strong melatonin receptor activity," *Horn*, page 4, line 13, which is a different mechanism from that of stimulating the expression of endothelial NO-synthase as claimed in the present invention. *See e.g.*, claims 6 and 12.

"In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." M.P.E.P. § 2112 (quoting *Ex parte Levy*, 17 U.S.P.Q.2d 1461, 1464 (Bd. Pat. App. & Inter. 1990)) (emphasis original). Further, to establish inherency, the Examiner bears the burden to provide extrinsic evidence, which "must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill." *Id.* (quoting *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999)); *see also* M.P.E.P. § 2131.02, III (quoting *Continental Can Co. USA v. Monsanto Co.*, 948 F.2d 1264, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991)). Here, the Office has not met its burden, failing to provide any basis in fact and/or technical reasoning to support its rejection based on inherent anticipation. Therefore, Applicants respectfully request these rejections be withdrawn.

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

IV. Rejection under 35 U.S.C. § 103(a)

The Office rejected claims 1 and 18-19 under 35 U.S.C. § 103(a) as being unpatentable over Albrecht et al., Chem. Abstract 77:88182 ("*Albrecht*"). Office Action, page 6. Specifically, the Office contended that *Albrecht* discloses substituted tetrahydronaphthalenyl compounds, which are structurally analogous to the presently claimed compounds, *i.e.*, positional isomers, because they are position-1 substituted tetrahydronaphthalenyl compounds, while the presently claimed compounds are position-2 substituted compounds. *See id.* The Office further contended that *Albrecht* disclosed that its compounds could be used as antimicrobial agents. *Id.* Therefore, the Examiner concluded, one of ordinary skill in the art "would have been motivated to prepare the instantly claimed compounds because such isomeric compounds are suggestive of one another and would be expected to share similar properties . . . *i.e.*, as therapeutic agents." *Id.*

Applicants have amended claim 1 to include an additional proviso that "in case groups A, B, and C are each CH_2, R^5 is not 5-nitrofuryl." Under this additional priviso, compounds claimed in the present invention are no longer positional isomers of the compounds disclosed in *Albrecht*. And claims 18 and 19 are dependent on claim 1. Therefore, Applicants respectfully request this rejection be withdrawn.

V. Allowable Subject Matter

The Office indicated that claim 5 "is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims." Office Action, page 7.

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

In response, Applicants have amended claim 5 to be in an independent form, and respectfully request claim 5 be allowed.

In addition, Applicants added new claims 30-36, which incorporated the compounds recited in claim 5. Therefore, Applicants respectfully request that claims 30-36 be allowed.

VI. Conclusion

In view of the foregoing claim amendments and remarks, Applicants respectfully request reconsideration and reexamination of this application, and the timely allowance of the pending claims.

If the Examiner believes a telephone conference could be useful in resolving any outstanding issues, he is respectfully urged to contact Applicant's undersigned counsel at 202-408-4218.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: September 22, 2003

By: _____
Ningling Wang
Reg. No. 52,412

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com